REMARKS/ARGUMENTS

Applicant acknowledges receipt of the Office Action dated October 2, 2003. Reconsideration and further examination of the claims is respectfully requested.

Claim Amendments

By present amendment, claim 1 has been amended to delete the phrase "the steps of," and to combine points 1-3. Support for this amendment is found on page 2, lines 18-21, of the application as filed. Claim 1 has been further amended to add that the reaction is performed without additional solid supports. Support for this amendment is found on page 2, lines 21-22, of the application as filed. Claims 9 and 10 have been canceled. Claim 11 is new and corresponds to original claim 1 wherein the term "comprising the steps of" has been replaced with the term "consisting essentially of." Support for this amendment is found on page 2, lines 21-22 of the application as filed.

The amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right to file any of the deleted subject matter in a further continuation, continuation-in-part or divisional application. No new matter has been entered by the present amendment.

The Official Action dated October 2, 2003 has been carefully considered. It is believed that the amended claims submitted herewith and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Claim Objections

35 USC §102(b): Anticipation

The Examiner has found claims 1-10 to be not novel in light of Jewett et al. (New Trends in Radiopharmaceutical Synthesis, Quality Assurance and Regulatory Control, Emran, A.M. Ed. pp. 387-391, 1991, hereinafter Jewett). The Examiner contends that Jewett discloses a method of radiolabeling a precursor compound comprising injecting into an injection loop of a HPLC a chemical precursor compound and a radiolabeling agent, allowing the precursor and radiolabeling agent to react and injecting into the HPLC column and isolating the compound. In response, the Applicants have amended claim 1, and therefore claims 2-8, dependent thereon, so that the method does not require the use of any additional solid supports.

The work by Jewett focused on using solid supports as the milieu in which the trapping and radiochemical reactions occurred (see, for example the Summary on page 387 of Jewett, where it is stated that "the reaction is done in a small volume of solvent absorbed in a porous solid matrix"; also on page 388, lines 3-6, Jewett states "This requires that the solvent containing the precursor be **restrained** during reaction with [^{11}C]-MeI but later be readily displaced by the chromatographic solvent" (emphasis added)). In contrast, the present invention is based on the observation that the milieu for the radiochemical process may simply be a tube capable of trapping, reacting, and delivering the product(s) to the purification system in a quantitative manner. In the present invention no solid supports were applied and the reacting materials were unfettered.

The disadvantages of Jewett's technique are two-fold:

A) The device containing the precursor, solvent, and base catalyst (if required) has to be assembled separately from the purification and delivery system, then installed into the main apparatus before each run (See page 389, lines 5-6: "injected slowly onto the column which was then installed in the HPLC system by Tefzel fingertight nuts"). With the present invention, no pre-assembly is required. The reagents are simply loaded into the apparatus by means of a syringe equipped with fine gauge needle.

B) Restraint of materials in a porous solid matrix is detrimental to purification methods. Release into the purification column is often not fast enough, which results in significant peak broadening, i.e. lower resolution. With no restraints, as in the present invention, transfer of materials from the reaction system (the loop) is almost instantaneous and results in no discernable peak broadening in the HPLC chromatogram.

The novelty and advantages of the method of the present invention can be further illustrated by the observation on page 391, lines 15-17, of Jewett that "Evaluation of this system by the colorimetric microassay for CH_3I showed little capture of the CH_3I by the system itself (<10%), but >90% capture when the substrate was added." In contrast, the present system traps >90% of CH_3I whether a substrate is present or not, thus allowing relatively unreactive substrates to be used, making the method universal and not just limited to highly reactive precursors.

Claims 9 and 10 have been canceled.

In light of the above amendments and arguments, the Applicants request that the Examiner's rejection of claims 1-10 under 35 USC §102(b) be withdrawn.

The Examiner has found claims 1-4, 6, 7, 9 and 10 to be not novel in light of Watkins et al. (Appl. Radiat. Isot. 39, pp. 441-444, 1988, hereinafter Watkins). The Examiner contends that Watkins discloses a method of radiolabeling a precursor compound comprising injecting into an injection loop of a HPLC a chemical precursor compound and a radiolabeling agent, allowing the precursor and radiolabeling agent to react and injecting into the HPLC column and isolating the compound. In response, the Applicants have amended claim 1, and therefore claims 2-4, 6 and 7 dependent thereon, so that the method does not require the use of any additional solid supports.

As with the work of Jewett, Watkins also describes the use of a "captive solvent method" for the preparation of radiolabeled chemical compounds. In Watkins, the reagents are absorbed onto acrylic yarn (see Watkins page 441, abstract), although it is stated that "a variety of synthetic fibers and microporous particles" (page 443, last line) may be used.

As stated above, the present inventors have found an efficient method for the preparation and purification of radiolabeled chemical compounds without the use of additional solid supports. Claim 1, and claims dependent thereon, have been amended to add that the reagents are reacted without additional solid supports, and accordingly are not anticipated by Watkins.

Claims 9 and 10 have been canceled.

In light of the above amendments and arguments, the Applicants request that the Examiner's rejection of claims 1-4, 6, 7, 9 and 10 under 35 USC §102(b) be withdrawn.

35 USC §103(a): Obviousness

The Examiner has found claims 1-10 to be obvious in light of Watkins in view of Dannals et al. (Quantitative Imaging: Neuroreceptors, Neurotransmitters and Enzymes, Frost, J.J. Wagner, Jr. H.N. Eds. pp. 19-35, 1990, hereinafter Dannals). The Examiner contends that it would have been obvious to one of ordinary skill in the art to use both an acid salt precursor and/or catalyst in the methods disclosed by Watkins, in particular in light of Dannals.

As noted above, claim 1, and therefore claims dependent thereon, have been amended so that the method does not require the use of any additional solid supports. The advantages of the method of the present invention have been delineated above. The Applicants submit that there is no motivation in Watkins or Dannals, alone or in combination, to perform a method of preparing a radiolabeled chemical compound in the injection loop of an HPLC without the use of additional solid supports, therefore the present invention as presented in claims 1-8 and 11, submitted herewith, would not have been obvious to a person skilled in the art.

In light of the above arguments, the Applicants request that the Examiner's rejection of claims 1, 2 and 16 under 35 USC §103 (a), be withdrawn.

While we believe that the instant amendment places the application in condition for allowance, should the Examiner have any further comments or suggestions, it is respectfully requested that the Examiner telephone the undersigned attorney in order to expeditiously resolve any outstanding issues.

In the event that the fees submitted prove to be insufficient in connection with the filing of this paper, please charge our deposit account number 50-0578 and please credit any excess fees to such Deposit Account.

Respectfully submitted,
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